

Changing Clinical Pattern of Dengue Fever and its Unusual Manifestations- 2019 Outbreak in Dhaka, Bangladesh

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Abstract:

Background: In 2019 Bangladesh faced largest outbreak of Dengue fever (DF) and clinicians observed some changing patterns in presentation and laboratory findings of DF. This study intends to find the changing patterns of dengue and its different manifestations including unusual one.

Material and Methods: This study deals around 220 dengue patients visited to Popular Medical College Hospital as inpatient of medicine department during the period 1st July 2019 to 31st December 2019. Chi-square statistics was used find the intra and inter association among the disease manifestations and multinomial logistic regression analysis was used to compare disease severity.

Results: Among 220 dengue serologically positive cases, the most common age group affected was 18-49 years (68.6%). Regarding the known common features like

fever (91.8%), vomiting (50.2%), headache (48.2%), were frequent among the patients but myalgia (19.6%), rash (14.5%), retro orbital pain (14.1%) were not so common. Presence of unusual features like abdominal pain (49.3%), loose motion (55%) and cough/ breathlessness (41.4%) ascites (53.2%), pleural effusion (51.8%), hepatomegaly (32.3%), peri-gallbladder edema (35.5%) and splenomegaly (15.1%) were also common among dengue patients. Serum Lipase was also increased in (28.8%) cases suggesting pancreatitis.

Conclusion: Unusual Manifestations of dengue fever is common. As the spread of dengue is increasing with significant morbidity and mortality, it is extremely important for the clinicians to know about its unusual manifestations.

Keywords: Unusual manifestations; Diarrhoea; Breathlessness; Splenomegaly; Pancreatitis.

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Introduction:

Dengue fever (DF) is a highly endemic infectious disease of the tropical countries and is rapidly becoming a global burden. Globally, almost 50% of the population is estimated to be under risk resulting

in 390 million new dengue infections in each year¹. In the recent years, the incidence of dengue is increasing in developing countries with increased mortality. New onset of dengue cases in a dengue free area, clustering of cases, cases with atypical manifestations have made DF mandatory to get included under notifiable diseases.

Dengue is a tropical disease affected by single stranded RNA flavivirus spread by the bite of female *Aedes aegypti* and *Aedes albopictus* mosquitoes³. The virus has four sero-types namely, DEN-1, DEN-2, DEN-3 and DEN-4⁴. Infection with one sero-type gives lifelong immunity to same sero-type and temporary immunity to other sero-types⁴. Infection with multiple sero-types and secondary infections manifest severely than primary infections⁵. Dengue fever is usually a non-specific and self-limiting biphasic febrile illness. Clinical presentation of Dengue fever varies with a wide spectrum of signs

and symptoms. Infection can be asymptomatic or cause a range of severity from mild dengue fever to

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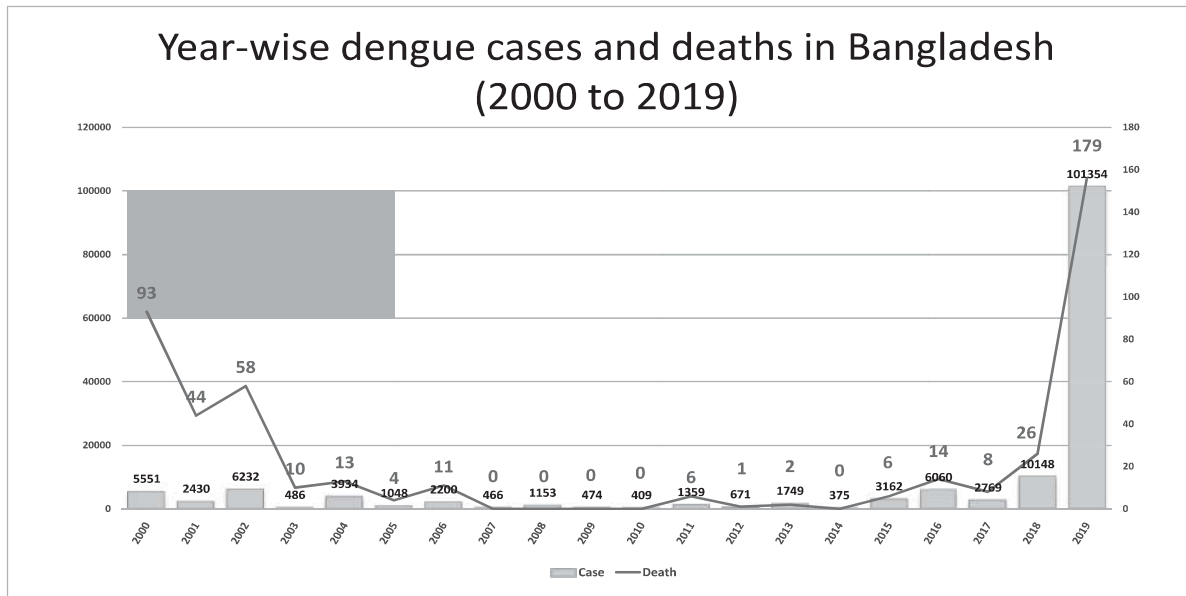
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dengue hemorrhagic fever, which can then progress to dengue shock syndrome and death⁶. Atypical manifestations are rare and include encephalopathy, encephalitis, seizures, hepatocellular damage, ARDS, acute renal failure, acalculous cholecystitis, myocarditis, pericardial effusion, severe gastrointestinal hemorrhage, Guillain-Barre syndrome and rhabdomyolysis^{7,8}.

Bangladesh first experienced a large outbreak of Dengue in the year 2000 with 5551 cases and case fatality was 93. The containment of the disease was successfully handled afterward and was rewarding. Even between the year 2007 to 2010 there were very lower number of cases reported with no death record. From 2015 the incidence of cases started rising with

few death This is obviously a change in epidemiology of the disease. Over 10,000 people, primarily in Dhaka, had been infected with the mosquito-borne disease in 2018. But strikingly in 2019 Bangladesh faced a nationwide outbreak affecting all districts² that began primarily in April. According to Director General of Health Services (DGHS), 101354 patients were affected and 179 died in 2019. With rising disease burden, atypical manifestations also noticed in many of the cases which are missed most often due to lack of awareness. Our aim of the study was to look for current patterns of the presentation along with unusual manifestations.



Source: Disease Control Room, DGHS, Mohakhali, Dhaka, January 2020

According to National Guideline for Clinical Management of Dengue Syndrome -2018, Dengue Case classified by severity into 3 groups-⁹

- i) Group-A: (Home Care): Patient who don't have a warning sign.
- ii) Group-B (Hospital Care): Patient with warning signs.
- iii) Group C: (must be hospitalized) Patient with any of the following features:
 - Severe plasma leakage with shock

or/and fluid accumulation with resp. distress

- Severe bleeding
- Severe organ impairment
- Severe metabolic dysfunction

Symptoms apart from the mentioned features are often co-existing. Many health care providers had expressed the need for expanding the list of atypical symptoms under typical dengue. Study aimed to search the varieties of symptoms of dengue and its unusual manifestations in 2019 outbreak.

Materials and Methods:

Ethics statement

Informed written consent had been taken from patients. They had the freedom to withdraw from the study at any time, if they desired.

It had been assured that all information and records would be kept confidential and the procedures would be helpful for both the physician and the patients in making rational approach to the care management. Privacy of the patients had been strictly maintained.

Study setting and design

This is a descriptive observational, record-based study done in the Department of Medicine, Popular Medical College and Hospital, Dhaka during July 1, 2019 to December 31, 2019. Total of 220 dengue patient's record who had dengue fever (DF) both clinical and lab confirmed - either by nonstructural protein1 (NS1) antigen positive or anti-dengue immunoglobulin M (IgM) antibody positive during this study period were included in this study. Dengue with comorbid conditions that may affect the outcome such as diabetes, hypertension, Pregnancy, menstruation was also included. Data had been entered in a standard proforma (Case Record Form) prepared by literature review and expert opinion. Dengue infection was classified according to National Guideline for Clinical Management of Dengue Syndrome -2018.

A detailed clinical history, physical examination and baseline investigations were undertaken and followed up till the patient got discharged from hospital. All clinical and laboratory details were carefully reviewed with daily assessment during hospital stay as per pre-tested questionnaire. The study includes demographic variables including age, sex and clinical diagnosis variables namely febrile diarrhea, abdominal pain, dyspnea, vomiting, pleural effusion, ascites, hepatomegaly, splenomegaly, gall bladder edema, rash, abdominal pain and investigational variables mainly ALT, AST. Out of above clinical diagnoses, unusual manifestations of dengue such as febrile diarrhea, gall bladder edema, abdominal pain, hepatomegaly, splenomegaly and increased lipase are considered for further study.

Statistical analysis

Data collected from the dengue patients were analyzed using Stata version 16. Categorical variables were expressed as frequencies

(percentages) and chi-square test was performed to find the significance of those variables. The patient's data were tabulated according to categorical variables including sex, clinical manifestations, comorbidity, radiological finding of DF, diagnostic and biochemical laboratory finding of DF. Continuous variables such as age, days of illness, SGOT (AST), SGPT (ALT), and lipase were also categorized. Any variable with $p \leq 0.05$ on chi-square analysis was considered statistically significant and then further analyzed in the multinomial logistic regression analysis to compare group B and group C relative to group A for severe clinical manifestations of dengue patients. This data was used to find the relationship between demography, clinical manifestations and laboratory parameters with severity of dengue patients. The analyses were performed at 95% confidence interval with $p < 0.05$.

Result:

Baseline characteristics of dengue patients

Among total 227 cases, 220 confirmed cases were evaluated. Due to insufficient data 7 cases were dropped from study. Among 220 confirmed cases, 118 (53.6%) were male and 102 (46.4%) were female. Majority of the cases 151 (68.6%) were from the age group of 18 to 49 years old. Age group < 18 years and age group 50 years and above were found 32 (14.6%) and 37 (16.8%) respectively.

(Table 1).

Most common clinical features were found as fever 202(91.8%), vomiting 110 (50.2%), headache 106 (48.2%), myalgia 43 (19.6%), abdominal pain 108 (49.3%), rash 32 (14.5%), retro orbital pain 31 (14.1%), hypotension 29 (13.2%), low pulse pressure 36(16.4%). Others symptoms included loose motion 121 (55%), cough/ breathlessness 91 (41.4%), bleeding 27 (12.3%), bradycardia 12 (5.5%) were also present. Comorbidities were reported among 76 patients including hypertension 27 (12.3%), diabetes 31 (14.1%), pregnancy 8 (3.6%) and menstruation 10 (4.6%). Most of the patient were Dengue NS1 positive 202(91.8%) but about 18(8.2%) cases were Dengue NS1 negative which were tested within 5 days of febrile episodes and later confirmed by Dengue -IgM positive test. Among 220 cases about 90 (40.9%) cases were dengue-IgG positive and 78 (35.5%) were dengue-IgM positive. Ascites and pleural effusion

Table 1: Demographic characteristics and distribution of dengue fever using the data set from Popular Medical College and Hospital during the period July 1, 2019 to December 31, 2019.

Characteristics	Total patients N=220	Distribution of dengue fever			P-value
		Group A (72)	Group B (111)	Group C (37)	
	N (%)	N (%)	N (%)	N (%)	
<i>Sex</i>					
Male	118 (53.6)	41 (34.8)	49 (41.5)	28 (23.7)	0.003
Female	102 (46.4)	31 (30.4)	62 (60.8)	9 (8.8)	
<i>Age</i>					
<18	32 (14.6)	13 (40.6)	11 (34.4)	8 (25.0)	0.038
18-49	151 (68.6)	53 (35.1)	74 (49.0)	24 (15.9)	
50 or above	37 (16.8)	6 (16.2)	26 (70.3)	5 (13.5)	
<i>Days of illness</i>					
Day 0	2 (0.9)	1 (50.0)	0 (0.0)	1 (50.0)	0.301
Day 2	6 (2.7)	1 (16.7)	3 (50.0)	2 (33.3)	
Day 3	24 (10.9)	6 (25.0)	15 (62.5)	3 (12.5)	
Day 4	50 (22.7)	16 (32.0)	24 (48.0)	10 (20.0)	
Day 5	68 (30.9)	18 (26.5)	24 (48.0)	14 (20.6)	
Day 6	51 (23.2)	20 (39.2)	36 (52.9)	4 (7.8)	
Day 7 +	19 (8.6)	10 (52.6)	27 (52.9)	3 (15.8)	

were very frequent on radiology report, which were respectively 117 (53.2%) and 114 (51.8%). Besides, hepatomegaly 71 (32.3%), splenomegaly 33 (15.1%) and gallbladder edema 78 (35.5%) were also common among dengue patients. Alanine transaminase (ALT)<100 U/L and ALT within 100-500U/L were found in a larger proportion of patients 114 (51.8%) and 79 (35.9%) respectively compared to Aspartate transaminase(AST)<100 U/L and AST within 100-500U/L 75 (34.1 %) and 69 (31.4%) respectively. But, AST > 1000 U/L and AST within 500-1000U/L were found in higher proportion of patients 32 (14.5%) and 44 (20.0%) respectively compared to ALT> 1000 U/L and ALT within 500-1000U/L 11 (5.0%) and 16 (7.3%). Lipase was increased in 63(28.8%) cases (Table 2).

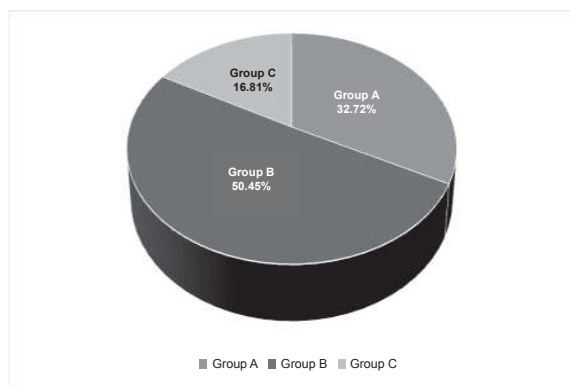


Figure 1: Distribution of dengue cases by group of severity among study population.

Findings by classification of groups according to “National Guideline for Clinical Management of Dengue Syndrome -2018”

Total 220 dengue patients were classified according to “National Guideline for Clinical Management of Dengue Syndrome -2018”, by severity into 3 groups as: Group A (low), Group B (mild/moderate) and Group C (severe). The total number of patients in group B were found higher 111 (50.45%) compared to group A 72 (32.72%) and group C 37 (16.81%) (Figure 1). A significant relationship was detected between gender and dengue classification groups (p = 0.003). Dengue infections were observed more frequently in group B both male 49 (41.5%) and female 62 (60.8%) individuals. Notably, male patients more frequently developed severe dengue 28 (23.7%) compared to female patients 9 (8.8%) (Figure 2).A significant relationship was detected between age group and dengue classification groups (p = 0.038) at 5% level of significance. Dengue infection was observed more frequently in age group < 18 years who were classified into group A(40.6%). Most of the patients belong to group B at the age group 18- 49 years 74 (49.0%) and age group 50 and above 26(70.3%) (Table 1).

Table 2: Clinical characteristics and distribution of dengue fever using the data set from Popular Medical College and Hospital during the period July 1, 2019 to December 31, 2019.

Characteristics	Total patients (220)	Distribution of dengue fever			P-value
		Group A (72)	Group B (111)	Group C (37)	
	N (%)	N (%)	N (%)	N (%)	
<i>Clinical manifestation</i>					
Fever	202 (91.8)	59 (29.2)	107 (53.0)	36 (17.8)	0.001
Vomiting	110 (50.2)	22 (20.0)	59 (53.6)	29 (26.4)	<0.001
Headache	106 (48.2)	38 (35.8)	55 (51.9)	13 (12.3)	0.200
Loose motion	121 (55)	18 (14.9)	73 (60.3)	30 (24.8)	<0.001
Pain abdomen	108 (49.3)	20 (18.5)	54 (50.0)	34 (31.5)	<0.001
Cough	91 (41.4)	12 (13.2)	55 (60.4)	24 (26.4)	<0.001
Rash	32 (14.5)	3 (9.4)	14 (43.8)	15 (46.9)	<0.001
Bleeding	27 (12.3)	2 (7.4)	8 (29.6)	17 (63.0)	<0.001
Retro-orbital pain	31 (14.1)	13 (41.9)	13 (41.9)	5 (16.2)	0.481
Hypotension	29 (13.2)	1 (3.4)	4 (13.8)	24 (82.8)	<0.001
Bradycardia	12 (5.5)	2 (16.7)	4 (33.3)	6 (50.0)	0.007
Low pulse pressure	36 (16.4)	8 (22.2)	9 (25.0)	19 (52.8)	<0.001
Myalgia	43 (19.6)	17 (39.5)	21 (48.8)	5 (11.7)	0.440
<i>Co-morbidity</i>					
Hypertension	27 (12.3)	3 (11.1)	20 (74.1)	4 (14.8)	0.020
Diabetes	31 (14.1)	3 (9.7)	24 (77.4)	4 (12.9)	0.003
Pregnancy	8 (3.6)	0 (0.0)	7 (87.5)	1 (12.5)	0.079
Menstruation	10 (4.6)	0 (0.0)	7 (70.0)	3 (30.0)	0.122
<i>Radiological finding of DF</i>					
Hepatomegaly	71 (32.3)	1 (1.4)	46 (64.8)	24 (33.8)	<0.001
Splenomegaly	33 (15.1)	1 (3.0)	9 (27.3)	23 (69.7)	<0.001
Gallbladder edema	78 (35.5)	3 (3.85)	50 (64.1)	25 (32.0)	<0.001
Ascites	117 (53.2)	5 (4.3)	81 (69.2)	31 (26.5)	<0.001
Pleural effusion	114 (51.8)	3 (2.6)	80 (70.2)	31 (27.2)	<0.001
<i>Diagnostic and biochemical laboratory finding of DF</i>					
NSI positive	202 (91.8)	66 (32.7)	101 (50.0)	35 (17.3)	0.785
Dengue Ig M Positive	78 (35.5)	21 (26.9)	44 (56.4)	13 (16.7)	0.351
Dengue Ig G Positive	90 (40.9)	16 (17.8)	54 (60.0)	20 (22.2)	<0.001
<i>SGOT (AST)</i>					
High (<100 U/L)	75 (34.1)	57 (76.0)	15 (20.0)	3 (4.0)	
100-500 U/L	69 (31.4)	13 (18.8)	53 (76.8)	3 (4.4)	<0.001
500-1000 U/L	44 (20.0)	1 (2.3)	36 (81.8)	7 (15.9)	
>1000 U/L	32 (14.5)	1(3.1)	7 (21.9)	24 (75.0)	
<i>SGPT (ALT)</i>					
High (<100 U/L)	114 (51.8)	69 (60.9)	39 (33.9)	6 (5.2)	
100-500 U/L	79 (35.9)	1 (1.3)	68 (86.1)	10 (12.7)	<0.001
500-1000 U/L	16 (7.3)	1 (6.2)	3 (18.8)	12 (75.0)	
>1000 U/L	11 (5.0)	1 (9.1)	1 (9.1)	9 (81.2)	
<i>Lipase</i>					
High (> 300 U/L)	63 (28.8)	2 (3.2)	32 (50.8)	29 (46.0)	<0.001

Clinical manifestations of dengue infection demonstrated that patients classified with group B were more frequently present with fever ($p = 0.001$), vomiting ($p < 0.001$), loose motion ($p < 0.001$), abdominal pain ($p < 0.001$), cough ($p < 0.001$), headache ($p = 0.200$), retro-orbital pain ($p = 0.481$), myalgia ($p = 0.440$). Clinical manifestations of dengue patients classified with Group-C were more frequently present with rash ($p < 0.001$), bleeding ($p < 0.001$), hypotension ($p < 0.001$), bradycardia ($p = 0.007$), low pulse pressure ($p < 0.001$). A significant relationship was found between diabetes ($p = 0.003$) and hypertension ($p = 0.020$) with dengue classification group. Those were highly occurred in group B. Relatively high proportion of group B dengue infected patients suffered from hepatomegaly ($p < 0.001$), gallbladder edema ($p < 0.001$), ascites ($p < 0.001$), pleural effusion ($p < 0.001$) and high proportion of group C patients suffered from splenomegaly ($p < 0.001$). A significant result was found between dengue IgG positive and dengue

classification group ($p < 0.001$). IgG positive result was observed more frequently in group B 54 (60%). In spite of giving insignificant result, most of the group B patients were observed giving Dengue IgM positive 44 (56.4%) and NS1 positive result 101 (50.0%). A significant result was found between dengue classification group and aspartate transaminase (AST) ($p < 0.001$) and alanine transaminase (ALT) ($p < 0.001$). A high proportion of patients with AST < 100 U/L was found in group A, AST (100-500 U/L) and AST (500-1000 U/L) were found highly in group B and AST (> 1000 U/L) was found highly in group C. Also for ALT, a high proportion of patients with ALT < 100 U/L was found in group A, ALT (100-500 U/L) was found highly in group B and ALT (500-1000 U/L) and ALT (> 1000 U/L) were found highly in group C. A significant result was found between dengue group and lipase (> 300 U/L) ($p < 0.001$) and a high proportion of patients were found in group B (Table 2).

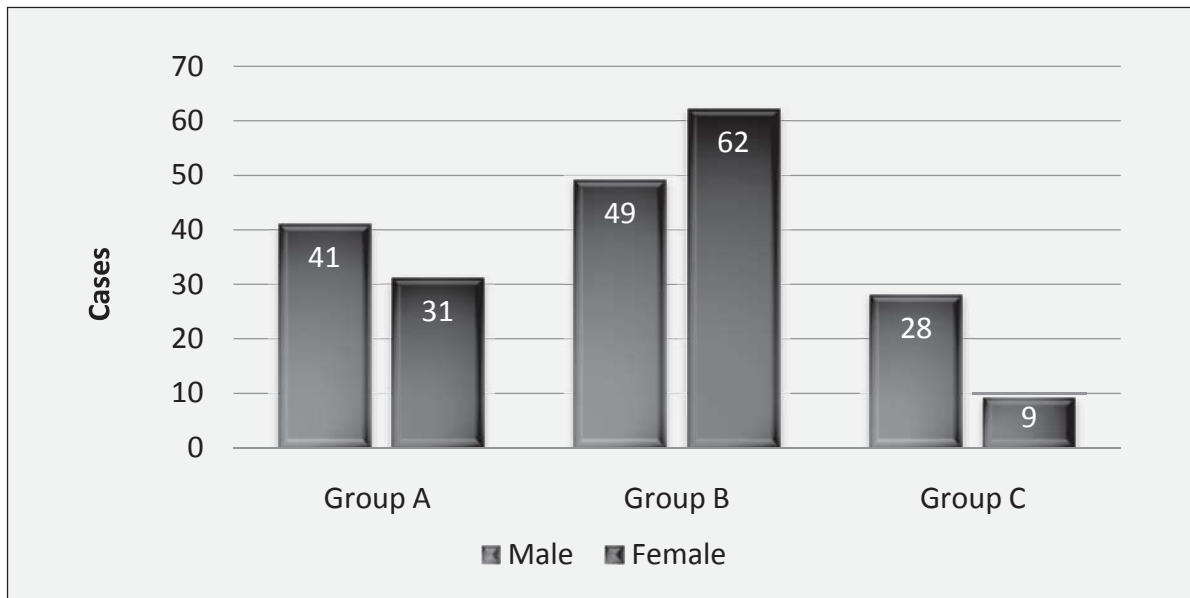


Figure 2: Gender differentiation with Group of Dengue cases.

Multinomial logistic regression model

Table 3 summarized the multinomial logistic relative odds ratio (ROR) estimate of group B and group C relative to group A dengue patients.

Comparison of group B relative to group A

The relative odds of being in group B rather than in group A for having cough was significantly 4.25 (ROR: 4.25, 95%CI: (1.02, 17.73); p value=0.047)

times or $(4.25 - 1) * 100\% = 325\%$ higher than the corresponding relative odds for not having cough keeping all other covariates at fixed level.

The relative odds of being in group B rather than in group A for having rash was significantly 12.14 (ROR:12.14, 95% CI: (1.62, 91.28); p value = 0.015) times or $(12.14 - 1) * 100\% = 1114\%$ higher than the corresponding relative odds for not having rash keeping all other covariates at fixed level.

Table 3: Multinomial logistic regression model using the data set from Popular Medical College and Hospital during the period July 1, 2019 to December 31, 2019.

Characteristics	Group B		Group C	
	ROR (95% CI)	P value	ROR (95% CI)	P value
Group A (Base Outcome)				
Gender				
Female	1.43 (0.41, 5.11)	0.574	1.003 (0.02, 39.05)	0.10
Age group				
18-49	1.32 (0.18, 9.52)	0.779	0.03 (3.2 e-05, 23.55)	0.297
50 or above	2.45 (0.17, 35.4)	0.509	0.02 (7.49e-07, 457.2)	0.439
Fever				
Yes	3.75 (0.29, 47.21)	0.306	0.04 (4.87e-07, 4332.9)	0.598
Vomiting				
Yes	1.33 (0.34, 5.21)	0.673	58.61 (0.14, 23747.7)	0.184
Loose motion				
Yes	3.18 (0.89, 11.35)	0.074	0.89 (0.01, 77.01)	0.962
Pain Abdomen				
Yes	0.84 (0.19, 3.53)	0.808	166.95 (0.27, 103069.1)	0.119
Cough				
Yes	4.25 (1.02, 17.73)	0.047	30.72 (0.56,1669.94)	0.093
Rash	12.14 (1.62, 91.28)			
Yes		0.015	359.41 (1.98,65072.0)	0.027
Bleeding				
Yes	1.55 (0.10, 22.62)	0.750	135.52 (0.11,161279.6)	0.174
Hypotension				
Yes	3.99 (0.01, 1278.1)	0.638	627.88 (0.51,771766.7)	0.076
Bradycardia				
Yes	2.42 (0.07, 86.32)	0.627	31118.2 (2.04,4.75e+08)	0.035
Low pulse pressure				
Yes	0.55 (0.07, 3.96)	0.553	8.93 (0.24, 338.67)	0.238
Hypertension				
Yes	1.84 (0.10, 33.41)	0.679	0.42 (5.7e06, 30836.4)	0.879
Diabetes				
Yes	3.22 (0.22, 47.14)	0.393	1.95 (0.002, 1728.03)	0.847
Dengue Ig G				
Yes	1.22 (0.32, 4.64)	0.772	0.84 (0.03, 26.82)	0.922
Hepatomegaly				
Yes	6.85 (0.46, 102.34)	0.163	21.16 (0.35, 1269.16)	0.144
Splenomegaly				
Yes	4.15 (0.17, 101.30)	0.382	11192.2 (2.78,4.50e+07)	0.028
Gallbladder edema				
Yes	1.81 (0.19, 17.25)	0.606	177.5 (0.125, 251445.4)	0.162
Ascites				
Yes	5.55 (1.12, 27.50)	0.036	75.17 (0.03, 159403.5)	0.269
Pleural effusion				
Yes	15.00 (2.36, 95.22)	0.004	5.72 (0.15, 217.60)	0.347
SGOT (AST)				
100-500 U/L	9.64 (3.84, 24.20)	<0.001	4.25 (0.72, 24.98)	0.109
500-1000 U/L	9.54 (0.44, 206.28)	0.150	58.28 (1.54, 2204.44)	0.028
>1000 U/L	3.29 (0.09, 125.92)	0.521	85.56 (1.45, 5046.25)	0.032
SGPT (ALT)				
100-500 U/L	35.75 (3.52, 362.58)	0.002	3.06 (0.11, 82.61)	0.506
500-1000 U/L	1.07 (0.02, 44.77)	0.970	0.52 (0.01, 31.84)	0.752
>1000 U/L	0.19 (0.003, 10.59)	0.418	0.19 (0.002, 14.63)	0.453
Lipase				
High (> 300 U/L)	14.15 (1.45, 137.41)	0.022	35.21 (3.23, 383.64)	0.003

The relative odds of being in group B rather than in group A for having ascites was significantly 5.55 (ROR:5.55, 95% CI: (1.12, 27.50); p value = 0.036) times or $(5.55 - 1) \times 100\% = 455\%$ higher than the corresponding relative odds for not having ascites keeping all other covariates at fixed level.

The relative odds of being in group B rather than in group A for having pleural effusion was significantly 15.00 (ROR: 15.00, 95% CI: (2.36, 95.22), p value = 0.004) times or $(15 - 1) \times 100\% = 1400\%$ higher than the corresponding relative odds for not having pleural effusion keeping all other covariates at fixed level.

The relative odds of being in group B rather than in group A for having AST (100-500 U/L) was significantly 9.64 (ROR: 9.64, 95% CI:(3.84, 24.20); p value < 0.001) times or $(9.64 - 1) \times 100\% = 864\%$ higher than the corresponding relative odds for AST (> 100 U/L) keeping all other covariates at fixed level.

The relative odds of being in group B rather than in group A for having ALT (100-500 U/L) was significantly 35.75 (ROR: 35.75, 95% CI: (3.52, 362.58), p value = 0.002) times or $(35.75 - 1) \times 100\% = 3475\%$ higher than the corresponding relative odds for ALT (> 100 U/L) keeping all other covariates at fixed level.

The relative odds of being in group B rather than in group A for having lipase (> 300 U/L) was significantly 14.15 (ROR: 14.15, 95% CI: (1.45, 137.41), p value = 0.022) times or $(14.15 - 1) \times 100\% = 1315\%$ higher than the corresponding relative odds for lipase (< 300 U/L) keeping all other covariates at fixed level.

Comparison of group C relative to group A

For multinomial logistic relative odds ratio (ROR) estimate of group C relative to group A dengue patients, clinical symptoms followed by rash (ROR: 359.41 95%CI: (1.98,65072.0); p value = 0.027), bradycardia (ROR: 31118.2,95% CI: (2.04,4.75e+08); p value = 0.035), splenomegaly (ROR: 11192.2,95% CI: (2.78,4.50e+07); p value = 0.028), AST 500-1000 U/L (ROR: 58.28, 95% CI: (1.54, 2204.44); p value =0.028), AST >1000U/L (ROR: 85.56, 95% CI: (1.45, 5046.25); p value =0.032), lipase (>300 U/L) (ROR: 35.21, 95% CI: (3.23, 383.64); p-value = 0.003) were statistically significant and can be interpreted like before group B relative to group A (Table 3).

Discussion:

In 2019, outbreak of dengue fever was unpredictable along with varieties of presentations. This study describes the clinical features, laboratory findings and radiological finding of DF. The maximum number of dengue cases in our study was seen in the months of July to November which indicated an active viral transmission during monsoon and post-monsoon period. This correlated with a study conducted by Gupta¹⁰ and UkeyP¹¹.

In a study done by the European Centre for Disease Prevention and Control, the case rate was ratio of 1. Similar in males and females, with a male-to-female 14:1.¹² Studies done by the WHO Western Pacific region showed a male preponderance in cases reported from Asia in contrast to the studies done in South America where it has been reported in equal proportions of male and female dengue cases or a greater proportion of female cases¹². In our study, the male patients slightly outnumbered the female patients and the male-to-female ratio was 1.16:1. But notably, male patients more frequently developed severe dengue (23.7%) compared to female patients (8.8%).

In our study, most of the patients were in the age group of 18–49 years (68.6%). Dengue infections were observed more frequently in age group < 18 years belonged to group A(40.6%). Most of the patients belonged in group B at the age 18- 49 years (49.0%) and age 50 and above (70.3%).

Typical manifestations of dengue fever are acute febrile illness with chills, body aches, myalgia, joint pain, petechial rash and bleeding manifestations. Several studies of travelers or military people have reported these “classic” symptoms of dengue fever in 15%–60% of patients^{13,14}. Regarding clinical finding in our study the known common features like fever (91.8%), vomiting (50.2%), headache (48.2%), were frequent among the dengue patients, these findings are similar to the findings of Jain D et al¹⁵. But myalgia (19.6%), rash (14.5%), retro orbital pain (14.1%) were not so common in this outbreak. Presence of hypotension (13.2%), narrow pulse pressure (16.4%) and some unusual feature like abdominal pain (49.3%), loose motion (55%) and cough/ breathlessness (41.4%) were predominant. Notable clinical and radiological findings were ascites and pleural effusion, respectively (53.2%) and (51.8%). Hepatomegaly and peri-gallbladder edema were also common which were respectively (32.3%)

and (35.5%)¹⁵. In 2019 outbreak some patients with dengue fever also presented with splenomegaly which was about (15.1%). Clinical manifestations of dengue infection demonstrated that patients classified with group B were more frequently presented with typical symptoms as fever, retro-orbital pain, headache, myalgia and also with atypical presentations including vomiting, loose motion, abdominal pain, cough..

Patients classified with group B & C were more prone to develop rash, bleeding, hypotension, bradycardia, low pulse pressure.

The hallmark of DF is fever. But few of our patients were afebrile and they were elderly. These afebrile Dengue could be the future challenge for detecting early complications of DF.

A significant relationship was found between diabetes ($p = 0.003$) and hypertension ($p = 0.020$) with dengue classification group. Those were highly occurred in group B.

Rapid diagnostic test Dengue NS1 is still the choice to detect early DF. In this study, about 18 cases were NS1 negative within 5 days of febrile episode and were later diagnosed by positive Dengue IgM test. These 18 patients had features of DF with fall in platelet count.

About 40.9% patient had Dengue –IgG positive within 7 days of onset of illness which indicated past infection. These patients undergone longer course with complications and most of them were categorized into group B and C (P value was highly significant $<.001$). So early detection of IgG may be helpful to predict the course of illness. These findings is near similar to a Caribbean study (85.7%) where cases had IgG positive on admission¹⁶. Mild to moderate rise in ALT and AST was found in a larger number of cases and high rise of ALT and AST were not very uncommon. In our study anicteric hepatitis was a common association in DF in 2019. Lipase was also increased in 28.8% cases suggesting pancreatitis is not an uncommon feature in DF.

Conclusion:

Dengue epidemics are on the rise in Bangladesh for last few years. Every monsoon brings along an outbreak of dengue. The last outbreak in 2019 was struck with an unexpected death. Though DF is a known disease to us, the clinicians observed some changes in patterns of presentation, along with severity of DF. A study like ours is a step forward to

detect the pattern of presentation in terms of usual and unusual features, disease course and severity. However, dengue virus serology would have helped us to correlate clinical manifestations with virus subtype. Among the findings notable was, a common finding myalgia was not so common this time. Febrile diarrhea, Pain abdomen, pleural effusion, ascites, gall bladder edema, hepatomegaly and splenomegaly were observed more common than before. Acute liver injury with elevated AST and ALT were significant. We found few afebrile DF and most of the severe cases were re infection as evidenced by early IgG positive. As the spread of dengue and dengue hemorrhagic fever is increasing with significant mortality and /morbidity, it is extremely important to consider atypical manifestations of dengue for appropriate diagnosis and treatment.

This would aid in the providing early treatment, and better care to the patients and further studies are needed to identify any specific serotype which may be responsible for the atypical manifestations.

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